

ORIGINAL ARTICLE

Nitrous oxide analgesia during intra-articular injection for juvenile idiopathic arthritis

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Aims: To evaluate the efficacy and safety of nitrous oxide–oxygen for children with juvenile idiopathic arthritis (JIA) undergoing intra-articular corticosteroid injection.

Methods: A total of 55 consecutive patients with JIA undergoing intra-articular corticosteroid injection, using self administered nitrous oxide–oxygen for analgesia were studied. Patient, nurse, and parent pain scores were compared using a 0–10 cm visual analogue scale (VAS) immediately after the procedure.

Results: A total of 70 joints were injected in 55 patients (median age 13.54 years). The median pain score for patient, nurse, and parent was 1 (0–10 cm VAS). The mean rank patient score was 2.12, which was greater than the nurse score (1.97), which was greater than the parent score (1.91). These differences were significant. There were no serious adverse events in any patient.

Conclusions: Nitrous oxide–oxygen provides safe and effective analgesia for intra-articular injection in children. In some cases, nurses and parents underestimated pain related to the procedure compared to the child.

Inhaled nitrous oxide at a concentration of 30–70% in oxygen has been used to alleviate pain associated with a variety of procedures in children, such as laceration repair,¹ gastro-intestinal endoscopy,² venous cannulation,³ and burns dressing.⁴ A recent national survey of the use and safety of inhaled nitrous oxide in France evaluated prospectively the procedure characteristics, pain evaluations, and adverse effects in 1019 painful procedures, including lumbar puncture, bone marrow aspiration, minor procedures, minor surgery, fractures, dental care, and pulmonary endoscopy.⁵ The nitrous oxide–oxygen was tolerated in 87.3% of procedures, with optimum results in children 3 years of age and older.

The behavioural response of children undergoing a painful procedure using inhaled nitrous oxide–oxygen have been assessed using the Observational Scale of Behavioural Distress—Revised.⁶ Children over the age of 6 years showed a lower level of distress, with the additional benefit of procedural amnesia reported in 65% of subjects. There have been no serious adverse effects associated with the use of inhaled nitrous oxide–oxygen mixture. Common adverse effects reported include euphoria, nausea and vomiting, clinically insignificant hypoxia, abnormalities of peripheral sensation, dizziness, restlessness, and hallucinations.^{5,6} All were transient, with recovery time less than five minutes.

We report here our experience with the use of nurse supervised self administered nitrous oxide–oxygen mixture during intra-articular steroid injection in 55 children with juvenile idiopathic arthritis (JIA). The use of nitrous oxide–oxygen in this setting was prompted by perceived problems associated with the use of intravenous sedation with benzodiazepines, including patient distress during venous cannulation, failure to achieve adequate hypnotic effect, and potential risk of serious adverse effect including respiratory depression. In order to objectively assess the efficacy and safety of nitrous oxide–oxygen inhalation in our units we performed a prospective study of intra-articular injections in children with JIA.

PATIENTS AND METHODS

All children over the age of 7 years with JIA listed for intra-articular injection in two paediatric rheumatology

centres were studied. Patients were selected consecutively and providing they were capable of self administration of the nitrous oxide–oxygen mixture there were no exclusion criteria. In each centre the intra-articular injection was performed by the same physician. The inhalation of the nitrous oxide–oxygen mixture was supervised by nursing staff on a paediatric hospital day case unit, following locally approved guidelines. The nurse supervising the administration of nitrous oxide–oxygen had been trained and assessed in this expanded role according to local guidelines. A second nurse was present to assist the physician. Nitrous oxide–oxygen was delivered as a fixed mixture of 50% nitrous oxide/50% oxygen (Entonox, BOC Gases). The gas was delivered by means of a mouthpiece connected through a demand valve (Sabre Medical Systems) and was patient administered. A bolus of Entonox could be administered by staff if they felt it was required. Distraction techniques were frequently employed, and where appropriate the play specialist was involved with the children before and during the procedure. The patients were not fasted prior to the procedure, but as most were on the day care ward for approximately one hour before the procedure, they were advised not to eat during this time. Fluid was available to drink on demand at all times during the sedation. Written consent for the procedure was obtained in all cases.

Topical anaesthesia (Ametop or EMLA) was applied prior to the procedure in all cases except for injection of a proximal interphalangeal (PIP) joint. Lignocaine (1%) was infiltrated subcutaneously (21 gauge needle) according to physician preference prior to joint puncture, and used to flush the needle after injection of the corticosteroid preparation. Triamcinolone hexacetonide was used for all intra-articular injection, except for the PIP joint, which was injected with hydrocortisone acetate. A 25 gauge needle was used to inject the PIP joint. All other joints were injected with a 21 gauge needle. The analgesic efficacy of the Entonox was assessed by means of a

Abbreviations: JIA, juvenile idiopathic arthritis; PIP, proximal interphalangeal; VAS, visual analogue scale

Table 1 Ages of patients with JIA using Entonox during intra-articular injection

Age (years)	Number of patients
<10	10 (18.2%)
10–13	13 (23.6%)
13–16	23 (41.8%)
16–18.78	9 (16.4%)

Table 2 Distribution of joints injected

Joint injected	Number
Knee	50
Ankle	16
Wrist	2
Elbow	1
Proximal interphalangeal joint	1

Table 3 Median pain scores with interquartile range

	Median (interquartile range) pain score 0–10 cm visual analogue scale
Patient	1 (2.75)
Nurse	1 (2.0)
Parent	1 (2.0)

0–10 cm visual analogue scale (VAS), completed by patient, nurse, and parent where appropriate.

Statistics

Data analysis was performed using standard software (SPSS for Windows 9.0). Pain scores were expressed as median with interquartile range. Differences between patient, nurse, and parent pain scores were tested using the Friedman non-parametric test for paired data. The Wilcoxon signed ranks test was used to test for differences between patient/nurse and patient/parent pain score.

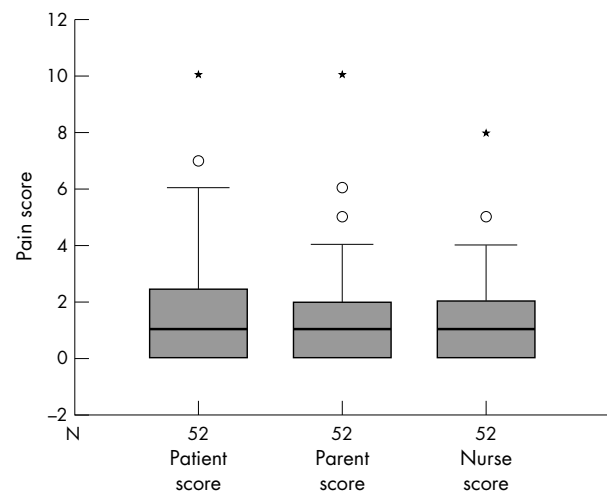
RESULTS

A pain assessment form was completed by 55 patients after intra-articular injection; 29 (52.7%) were female, 26 (47.3%) were male. Median age was 13.54 years (range 7.05–18.78). Table 1 gives the distribution of ages of the patients. A total of 70 joints were injected. Table 2 shows the distribution of injected joints.

Pain scores

At the end of each procedure the patient, nurse, and parent if present completed a 0–10 cm visual analogue pain score. Table 3 shows the median pain score with interquartile range. Figure 1 shows the pain scores as box and whisker plots.

The median pain score for patient, nurse, and parent was 1 on a 0–10 cm VAS. This is shown by the heavy line in fig 1. As the interquartile range is larger in the patient group, differences between the pain scores in each of the three groups were tested. The mean rank patient score was 2.12, which was greater than the nurse score (1.97), which was greater than the parent score (1.91). These differences were significant ($p = 0.031$). To determine where the differences were, the Wilcoxon signed ranks test (with Bonferroni correction) was

**Figure 1** Patient, parent, and nurse pain score.

applied to the parent score versus patient score and patient score versus nurse score. The patient score was greater than the parent score ($p = 0.032$), and the patient score was greater than the nurse score ($p = 0.048$).

Adverse events

No serious adverse events were observed in any patient. Six of 55 patients gave a pain score greater than or equal to 5. These patients were aged 8–18 years.

DISCUSSION

A fixed mixture of nitrous oxide and oxygen was introduced by Tunstall in 1961 for use during labour and childbirth.⁷ The use of nitrous oxide–oxygen mixture has subsequently spread into many areas including dental practice, the ambulance service, and for the alleviation of procedure related pain in a variety of hospital settings. This is the first prospective study of the use of Entonox in paediatric patients undergoing intra-articular corticosteroid injection for juvenile idiopathic arthritis.

The use of Entonox has dramatically reduced waiting time for intra-articular injection in our patients. It is significantly cheaper than general anaesthesia. There were no serious adverse events recorded. The patients were not monitored by pulse oximetry during sedation, but verbal contact was maintained throughout the procedure, and level of sedation scored according to local hospital guidelines. In the majority the Entonox was both well tolerated and efficacious, as shown by the median pain scores on a 0–10 cm VAS.

Prior to introducing Entonox for intra-articular injection in our practice, the procedure was carried out under sedation with intravenous midazolam. This had the disadvantage of requiring insertion of an intravenous cannula, which despite the use of topical anaesthesia was often a distressing procedure for the children. Subsequent sedation obtained was frequently less than adequate, and although no serious adverse events occurred, the potential for respiratory depression was much higher than for Entonox. Midazolam does however have a well recognised amnesic effect.

Disadvantages of Entonox include the presence of a mask or mouthpiece. We found a mask, even if scented, was more likely to induce a state of anxiety and nausea in the patient, hence the use of the mouthpiece. Adequate sedation was achieved in all despite the possibility of nasal breathing and dilution of the nitrous oxide component of the inhaled gas. The inhalation technique was rapidly acquired by most children.

Other non-pharmacological techniques utilised included distraction, music, relaxation, and the use of laser lights. The

youngest child in this study was 7 years, although it may be possible to use inhaled nitrous oxide–oxygen in younger children who are assessed on an individual basis. We feel that the play leader has an important function in helping the child adjust to the procedure, but obviously the approach taken will vary according to the needs of each individual. Adequate resuscitation equipment and trained personnel must, however, always be immediately available should a serious adverse event occur.

Pain is an unpleasant sensory and emotional experience, and is always subjective.⁸ Adequate management of pain in children requires the use of objective, reliable, and valid measures for assessing pain. A VAS has been validated as an excellent tool for measuring pain.⁹

It is interesting that there were group differences in pain scores. This warrants further investigation, and suggests that at times both nurse and parent underestimated the procedure related pain experienced by children in this study. It must be pointed out that of the 55 patients in the study, the nurse scored pain lower than the patient only in seven cases. The parent scored pain lower than the patient in seven cases also, although not necessarily the same cases as the nurse. Previous studies have also reported that nurses occasionally underestimate children's pain.^{5–10} Parents' pain scores for their children when undergoing procedures have been previously compared to those of their children. In a study of pain associated with immunisation in children aged between 4 and 6 years, parents underestimated their child's pain when using two of three different pain assessment tools.¹¹

In contrast, when the pain associated with JIA per se was assessed using the paediatric pain questionnaire,¹² Benestad *et al* found no significant differences between JIA patient, parent, and physician scorings of present and worse pain associated with arthritis.¹³ The correlation found between children's and parent's assessment of pain was low, and the median pain score reported by the child was lower than that of parent and physician. It is our experience that in the outpatient clinic the parent score for pain associated with their child's arthritis tends to be higher than that given by the child, in contrast to the results for procedure related pain reported in ours and other studies. The nature of a child's pain may be influenced by factors other than the intensity and duration of the nociceptive stimulus, such as cognitive, behavioural, and emotional factors.¹⁴ It seems likely that such factors are relevant in the assessment of procedure related versus disease related pain, and may account for differences between children's, nurses', and parents' perception of pain.

Despite the small number of children who scored pain higher than nurse or parent, it is our impression that Entonox facilitates intra-articular steroid injection, and this remains our preference in those children capable of the self administration technique. The possibility of underestimating the child's pain during the procedure is highlighted and needs future consideration.

Conclusion

When used for intra-articular injection in children, Entonox is both effective and safe. Although such data were not formally collected it is the author's impression from discussion with patients and their parents that the majority of patients in the age group studied would undergo subsequent intra-articular

injection using Entonox in the future rather than general anaesthesia. Care needs to be taken in the assessment of pain in children. In a small number of cases there appears to be differences between children's, nurses', and parents' perception of procedure related pain. Parents and professionals occasionally underestimate procedure related pain in children.

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EDITOR'S NOTE

We advise readers to consult a letter published in *eADC* in response to a previous study using nitrous oxide analgesia in children.* Nitrous oxide is contraindicated in patients with borderline of deficient vitamin B12 status. In her letter, Dr Smith points out that such children might include those with prolonged illness associated with poor feeding and increased metabolic demand.

* Smith I. Nitric oxide and vitamin B12 [electronic response to Kanagasundaram SA *et al*, Efficacy and safety of nitrous oxide in alleviating pain and anxiety during painful procedures], *archdischild.com*, 2001.<http://adc.bmjjournals.com/cgi/eletters/archdischild;84/6/492>.

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